

SHARED CARE GUIDELINES

Rivastigmine for the treatment of mild to moderate Alzheimer's disease

It is vital, for safe and appropriate patient care, that there is a clear understanding of where clinical and prescribing responsibility rests between Consultants and General Practitioners (GPs).

This guideline reinforces the basic premise that;

- When clinical and / or prescribing responsibility for a patient is transferred from the Wirral Memory Assessment Service (WMAS) to GP, the GP should have full confidence to prescribe the necessary medicines. Therefore, it is essential that a transfer of care involving medicines that a GP would not normally be familiar with, should not take place without the "sharing of information with the individual GP and their mutual agreement to the transfer of care."

These are not rigid guidelines. On occasions, Consultants and GPs may agree to work outside of this guidance. As always, the doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

Licensed indication:

Rivastigmine is licensed for the treatment of mild to moderate Alzheimer's dementia.

NICE Guidance recommends that treatment should only be prescribed under the following conditions:

- Alzheimer's disease must be diagnosed and treatment initiated by a specialist; treatment can be continued by general practitioners under a shared-care protocol;
- The carers' views of the condition should be sought before and during treatment;
- Treatment should continue only if it is considered to have a worthwhile effect on cognitive, global, functional, or behavioural symptoms.

Dosage and administration:

Please follow the Cheshire & Wirral Partnership NHS Foundation Trust, Mental Health Medicines Formulary;

First line

Donepezil

Second line

Rivastigmine capsules

Adults/Elderly:

- Orally, 1.5mg twice daily, increased in steps of 1.5mg twice daily at intervals of at least 2 weeks according to response and tolerance; usual range 3 to 6mg twice daily; max 6mg twice daily. It should be taken with food.

When administering the oral solution the prescribed amount should be withdrawn from the container using the oral dosing syringe supplied. It may be swallowed directly from the syringe. Oral solution and capsules may be interchanged at equal doses.

- Patch, apply 4.6mg/24 hours patch to clean, dry, non-hairy, non-irritated skin on back, upper arm, or chest. Remove after 24 hours and put new patch in a different area. It is not recommended to apply the transdermal patch to the thigh or to the abdomen due to decreased bioavailability. The transdermal patch should not be applied to skin that is red, irritated or cut. If well tolerated increase to 9.5mg/24 hours after at least 4 weeks.

N.B Rivastigmine patch and solution is restricted to those with swallowing difficulties. Rivastigmine patch is restricted to those unable to tolerate oral medication.

Patients and caregivers should be instructed on important administration instructions:

- The previous day's patch must be removed before applying a new one every day.

- The patch should be replaced by a new one after 24 hours. Press down firmly for at least 30 seconds until edges stick well. Only one patch should be worn at a time
- If the patch falls off, a new one should be applied for the rest of the day, then it should be replaced at the same time as usual the next day.
- The patch can be used in everyday situations, including bathing and during hot weather.
- The patch should not be exposed to any external heat sources (e.g. excessive sunlight, saunas, and solarium) for long periods of time or cut into pieces.

Third line

Galantamine tablets

• If donepezil is not prescribed the rationale for prescribing one of the alternative acetylcholinesterase inhibitors must be documented and details shared with the GP.

No dose adjustment is necessary for patients with mild to moderate renal or hepatic impairment. However, due to increased exposure in these populations dosing recommendations to titrate according to individual tolerability should be closely followed as patients with clinically significant renal or hepatic impairment might experience more adverse reactions. Patients with severe hepatic impairment have not been studied.

Children: Rivastigmine is not recommended for use in children and adolescents below 18 years of age.

Contra-indications: Known hypersensitivity to the active substance rivastigmine, to other carbamate derivatives or to any of the excipients and in severe liver impairment. Previous history of application site reactions suggestive of allergic contact dermatitis with rivastigmine patch.

Cautions: Skin application site reactions may occur with rivastigmine patch and are usually mild or moderate in intensity. Allergic contact dermatitis should be suspected if application site reactions spread beyond the patch size but more intense local reactions can occur.

Serious adverse reactions have occurred when the old patch has not been removed and a new one has been applied.

Contact with the eyes should be avoided after handling the patches. Hands should be washed with soap and water after removing the patch. In case of contact with eyes or if the eyes become red after handling the patch, rinse immediately with plenty of water and seek medical advice if symptoms do not resolve.

Care must be taken when using rivastigmine in patients with sick sinus syndrome or conduction defects (sino-atrial block, atrio-ventricular block)

Rivastigmine may cause increased gastric acid secretions. Care should be exercised in treating patients with active gastric or duodenal ulcers or patients predisposed to these conditions.

Cholinesterase inhibitors should be prescribed with care to patients with a history of asthma or obstructive pulmonary disease.

Cholinomimetics may induce or exacerbate urinary obstruction and seizures. Caution is recommended in treating patients predisposed to such diseases.

One of the excipients in Exelon oral solution is sodium benzoate. Benzoic acid is a mild irritant to the skin, eyes and mucous membrane.

The use of rivastigmine in patients with severe dementia of Alzheimer's disease or associated with Parkinson's disease, other types of dementia or other types of memory impairment (e.g. age-related cognitive decline) has not been investigated and therefore use in these patient populations is not recommended.

Like other cholinomimetics, rivastigmine may exacerbate or induce extrapyramidal symptoms. Worsening (including bradykinesia, dyskinesia, and gait abnormality) and an increased incidence or severity of tremor may occur in patients with dementia associated with Parkinson's disease.

The administration of rivastigmine concomitantly with other inhibitors of acetylcholinesterase, agonists or antagonists of the cholinergic system should be avoided.

For full information see the current edition of the British National Formulary (BNF)

Adverse effects:

For full information see the current edition of the British National Formulary (BNF).

The most common adverse effects are gastrointestinal including nausea and vomiting.

Common adverse events are asthenia, anorexia, dizziness, somnolence, abdominal pain, agitation, confusion, diarrhoea, dyspepsia, headache and weight loss.

Less Common increased sweating, malaise, fatigue, tremor and insomnia.

Report suspected adverse drug reactions via the Yellow Card Scheme, either online at <https://yellowcard.mhra.gov.uk/> or by using the yellow forms at the back of a current BNF

Monitoring requirements:

Because of the risk of bradycardia, the pulse must be monitored regularly, and discontinued immediately if the pulse falls below 50 beats per minute, or if there is evidence of developing heart block.

The NICE Health Technology Appraisal on these medications mandates the monitoring of cognition, and global functioning. The recommended scales for this locally are the Montreal Cognitive Assessment (MoCA, www.mocatest.org), Mini-Addenbrooke's cognitive Examination (mini-ACE) and the Global Deterioration Scale (GDS).

Practices will continue to monitor a patient's cognitive level, as per NICE guidelines, using the MoCA until certain criteria are met:

The patient is no longer able to complete this test, due to;

- Significant communication difficulties so that they can no longer understand the instructions for the test, or
- Experiencing significant distress as part of the testing process

The patient's cognitive level falls below 10/30 on this test

In these cases, the reason for the cessation of the cognitive testing must be recorded, and an overall assessment of the patient's condition made on the Global Deterioration Scale (GDS)

Action to be taken if abnormal results/adverse effects:

In the event of any adverse effects please contact the Wirral Memory Assessment Service (WMAS) for advice on 0151 488 7758. In the case of serious adverse events the medication should not be continued until that advice has been received.

Drug interactions: As a cholinesterase inhibitor, rivastigmine may exaggerate the effects of succinylcholine-type muscle relaxants during anaesthesia.

It should not be given concomitantly with other cholinomimetic substances and might interfere with the activity of anticholinergic medicinal products.

Metabolic interactions appear unlikely with rivastigmines.

For full information see the current edition of the BNF.

Specialist responsibilities:

1. Confirm the diagnosis of Alzheimer's disease following full assessment. Provide confirmation of this

- to the patient and carer, and communicate this to the referrer.
- 2. Ensure that baseline tests and investigations required have been provided by referrer.
- 3. Initiate and titrate rivastigmine for six months ensuring that the client is stable on the medication prior to transfer back to the referrer on the shared care protocol.
- 4. Monitor for side effects
- 5. Provide the referrer with details needed to continue the care of the client under the shared care protocol, to include details of the monitoring and prescriptions required for the client.
- 6. Review patients referred back to secondary mental health services through Single Point of Access if deterioration in behaviours or significant risks that cannot be safely managed by the Patient's GP.

- GP responsibilities:**
- 1. Initial referral to the Memory Clinic after an initial assessment that raises the possibility of dementia
This initial assessment should include a test of cognition, physical examination and the agreed initial investigations of Full Blood Count, Chemical Profile, Thyroid Function Tests, B12 and folate, and an up to date Electrocardiogram (ECG).
 - 2. Provide the patient with monthly repeat prescriptions of medication once the specialist has recommended continuation therapy following stabilisation. The patient should allow at least 48 hours for the prescription from the GP to be generated once they have agreed to take on prescribing.
 - 3. Review the patient every six months, including their pulse, cognitive assessment, global assessment, functional assessment, behavioural assessment, mental health and medication.
 - 4. Provide ongoing support and management for physical health issues
 - 5. Report any adverse effects of medication to consultant.
 - 6. Contact the specialist if they do not agree with the treatment recommendation or if there is a perceived problem with compliance or concordance, or if they have any questions about the management plan.
 - 7. Refer patient back to secondary care if deterioration in behaviours or significant risks. Refer on to appropriate agencies e.g. Social Services or the Alzheimer's Society (0151 630 5206) if additional support is needed for the client or their carer.

- Patient and parent/carer responsibilities:**
- Agree to request prescriptions from the GP in good time; obtain the first GP prescription within 2 weeks of being informed that shared care will be in operation.
 - Report any concerns or adverse effects to the GP or Pharmacist.

References: Summary of Product characteristics (SPC) for Exelon®
NICE Technology Appraisal – Donepezil, galantamine, rivastigmine & memantine for the treatment of Alzheimer's disease, issued March 2011 (TA217)
Drug Tariff online, March 2016

Availability: Primary care - please see Scriptswitch for most cost effective choices.
Rivastigmine 1.5mg capsules, 28 capsule pack
Rivastigmine 2mg/ml oral solution sugar free, 120ml bottle
Rivastigmine 3mg capsules, 28 capsule pack
Rivastigmine 4.5mg capsules, 28 capsule pack
Rivastigmine 4.6mg/24hrs transdermal patches, 30 patch pack
Rivastigmine 6mg capsules, 28 capsule pack
Rivastigmine 9.5mg/24hrs transdermal patches, 30 patch pack
Rivastigmine 13.3mg/24hrs transdermal patches, 30 patch pack

Back up advice and support - specialist	Telephone/Fax	Email address
Dr Andrew Ellis (Consultant Psychiatrist)	0151 488 8155	Andrew.Ellis@cwp.nhs.uk
Written By Dr Andrew Ellis, Consultant Psychiatrist	Abigail Cowan, Prescribing Adviser, Wirral Medicines Management Team (MLCSU)	